REMARKS

Claims 1-11 are pending. Claims 5, 6 and 9 are under examination. Claims 5 and 9 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendment to claim 5 can be found, for example, in paragraphs [0023], [00127-00128] and [00147]. Support for the amendment to claim 9 can be found, for example, in paragraph [0033]. The specification has been amended to correct typographical errors. Support for the amendments to the specification can be found in priority application serial No. 09/388,221. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Regarding the Sequence Listing

In the Office Action, it is indicated that brief description of Figures 1D and 1E does not include sequence identifiers and that it is unclear whether the Sequence Listing includes the sequences shown in Figures 1D and 1E. The specification has been amended to add sequence identifiers for the sequences shown in Figures 1D and 1E, SEQ ID NOS:19-30, respectively. The sequences corresponding to SEQ ID NOS:19-30 were included in the Sequence Listing filed August 23, 2004. Applicant respectfully submits that the application is in compliance with the requirements for disclosure of nucleotide and/or amino acid sequences under 37 CFR § 1.821-1.825.

Rejections Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 5, 6 and 9 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicant respectfully submits that the specification provides sufficient description and guidance for the claimed composition and methods.

Claim 5, as amended, is directed to a therapeutic composition comprising an effective amount of NB-ARC domain and CARD domain protein (NAC) modulating agent, wherein the agent alters the association of NAC and NAC associated protein (NAP) proteins and a pharmaceutically acceptable carrier, the NAC modulating agent identified by a method comprising a) contacting the NAC and NAP proteins, under conditions that allow the NAC and

NAP proteins to associate, with an agent suspected of being able to alter the association of the NAC and NAP proteins; and b) detecting the altered association of the NAC and NAP proteins, wherein the altered association identifies an effective therapeutic agent. Claim 9, as amended, is directed to a method of modulating transcription mediated by NFκB comprising contacting a cell with an agent, the agent identified by a method comprising a) contacting NAC and NAP proteins, under conditions that allow said NAC and NAP proteins to associate, with an agent suspected of being able to alter the association of said NAC and NAP proteins; and b) detecting the altered association of the NAC and NAP proteins, wherein the altered association identifies an effective agent that modulates transcription mediated by NFκB, wherein contacting the cell with the agent modulates transcription mediated by NFκB.

Applicant respectfully submits that the specification provides sufficient description and guidance for the claimed composition and methods. The specification teaches that a NAC can associate and bind relatively specifically to a protein to form a bound complex (paragraph [0035]). The specification also teaches that an agent is a chemical or biological molecule that has the potential to alter the association of a NAC with a heterologous protein or self-association (paragraph [00118]). An effective agent is indicated to be an agent that can alter the association of NAC with a heterologous protein or self association (paragraph [00118]). Furthermore, the claims recite functional activity of the agent. In particular, claim 5, as amended, recites that the agent alters the association of NAC and NAP proteins and further recites the method by which the agent is identified. Similarly, claim 9, as amended, recites that the agent alters the association of NAC and NAP proteins and is effective at modulating transcription mediated by NFκB. The specification additionally teaches the ability of NAC and NAP proteins to associate, as recited in the claims (see Examples, paragraphs [00176-00187]). Moreover, the specification teaches assay methods for identifying agents that modulate NAC activity, including altering the association of NAC and NAP proteins (see paragraphs [00125-00132]). Such assays include *in vivo* and *in vitro* assays, including, for example, yeast two hybrid and *in vitro* binding assays (see paragraphs [00125] and [00131]). Applicant respectfully submits that the specification provides sufficient description and guidance for the claimed composition and methods. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 5, 6 and 9 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicant respectfully submits that the specification provides sufficient description and guidance to enable the claimed composition and methods.

As discussed above, the specification teaches that a NAC can associate and bind relatively specifically to a protein to form a bound complex (paragraph [0035]). The specification also teaches that an agent is a chemical or biological molecule that has the potential to alter the association of a NAC with a heterologous protein or self-association (paragraph [00118]). An effective agent is indicated to be an agent that can alter the association of NAC with a heterologous protein or self association (paragraph [00118]). Furthermore, the claims recite functional activity of the agent. In particular, claim 5, as amended, recites that the agent alters the association of NAC and NAP proteins and further recites the method by which the agent is identified. Similarly, claim 9, as amended, recites that the agent alters the association of NAC and NAP proteins and is effective at modulating transcription mediated by NFκB. The specification additionally teaches the ability of NAC and NAP proteins to associate, as recited in the claims (see Examples, paragraphs [00176-00187]). Moreover, the specification teaches assay methods for identifying agents that modulate NAC activity, including altering the association of NAC and NAP proteins (see paragraphs [00125-00132]). Such assays include *in vivo* and *in vitro* assays, including, for example, yeast two hybrid and *in vitro* binding assays (see paragraphs [00125] and [00131]). Accordingly, Applicants respectfully submit that one skilled in the art could use routine assays to obtain the agents using the methods recited in the claims.

Applicant respectfully disagrees with the assertion in the Office Action on page 8 that the results described in paragraph [00187] highlight "the unpredictability inherent in the yeast two hybrid system." As taught in the specification, the yeast two hybrid assays were performed with the CARD domains of NAC ($CARD_L$) (paragraph [00179]), which was found to interact with caspase-9 (paragraph [00181]). The $CARD_L$ domain of NAC corresponds to amino acids 1128-1473 of SEQ ID NO:2 (paragraph [00175]). In the 293T transient transfection experiments referred to in paragraph [00187], the transfected NAC protein corresponded to amino acids 1-1261 and 1306-1473 of SEQ ID NO:2 (paragraph [00186]). In paragraph [00187], it is indicated that the results of the NAC not interacting with caspase-9 is in contrast with the interaction

observed between the $CARD_L$ domain of NAC and caspase-9 in the yeast two hybrid assay. This observation was indicated to may be due to the regulation of full length NAC in terms of its ability to interact with pro-caspase-9. Thus, comparison of the results observed with the $CARD_L$ domain of NAC binding to caspase-9 in the yeast two hybrid assay to those observed with full length NAC not binding to caspase-9 in the 293T cell transfection assays provides no basis for the assertion that yeast two hybrid assay results are inherently unpredictable, as asserted in the Office Action.

Regarding the therapeutic composition of claim 5, this claim, as amended, recites that the composition comprises an effective amount of a NAC modulating agent that alters association of NAC and NAP proteins. As taught in the specification, an "effective amount" is a predetermined amount calculated to achieve the desired therapeutic effect (see paragraph [00147]). The specification also teaches the treatment of various pathologies using therapeutic compositions (see paragraphs [00149-00151]). Furthermore, claim 5 specifically recites an effective amount, which as taught in the specification has the desired therapeutic effect. Accordingly, Applicant respectfully submits that the specification provides sufficient description and guidance to enable therapeutic compositions comprising an effective amount of a NAC modulating agent, wherein the agent alters the association of NAC and NAP proteins and a pharmaceutically acceptable carrier.

Applicant respectfully submits that the specification provides sufficient description and guidance to enable the claimed composition and methods. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claim 9 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Applicant respectfully submits that claim 9 is clear and definite. In the Office Action, it is asserted that claim 9 is unclear as to what transcription is being modulated. Claim 9, as amended, is directed to a method of modulating transcription mediated by NFκB. Applicant respectfully submits that claim 9 is clear with respect to the modulation of transcription. Accordingly, Applicant respectfully submits that claim 9 is clear and definite and respectfully requests that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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